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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,390	08/22/2001	Jaime Escobedo	PP-01369.103/200130.428C1	1981
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Chiron Corporation Intellectual Property R338 P.O. Box 8097 Emeryville, CA 94662-8097			MITRA, RITA	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/935,390

Applicant(s)

Jaime Escobedo

Examiner

Rita Mitra

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– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 1-7 and 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-12, 14-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1/15/2002.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicants' response to Restriction Requirement and preliminary amendment filed on March 29, 2004 is acknowledged. Applicants' election of Group III, claims 6-12, nucleic acid sequence SEQ ID NO: 4 and amino acid sequence SEQ ID NO: 23 in the reply filed on March 29, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-5 and 13-24 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. SEQ ID NO: 1-3, 5-19, 20-22, 24-38 have not been examined, SEQ ID NO: 4 and 23 have been examined. Claims 6-7 have been canceled and rewritten as new claims 14-24. Therefore, claims 8-12 and 14-24 are currently pending and are under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

“Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title”

Claims 8-12 and 14-24 are rejected under 35 U.S.C. 101 because the specification does not provide either a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention. The DNA in the construct for expressing all or a portion of a human protein and the nucleic acid in claims 14-24 are not supported by either a substantial asserted utility or a well established utility because the specification fails to assert any utility for the claimed DNA encoding the polypeptides and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed DNA encoding the polypeptide such that another non-asserted utility would be well established. Note, because the claimed invention is not supported by a substantial asserted utility for the reasons set forth above, credibility cannot be assessed.

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The specification, on pages 18-20, describes DNA constructs, for expressing all or a portion of a human protein in a host cell. The DNA construct comprises a promoter, which is functional in the particular host cell selected. The expression construct comprises a polynucleotide segment which encodes all or a portion of a human protein encoded by SEQ ID NO: 4. The polynucleotide segment is located downstream from the promoter. Transcription of the polynucleotide segment initiates at the promoter. The host cell comprising the DNA construct can be any suitable prokaryotic or eukaryotic cell. Further the specification indicates at page 20 that alternatively, expression of an endogenous gene encoding a protein of the invention can be manipulated by introducing by homologous recombination a DNA construct comprising a transcription unit in frame with the endogenous gene, to form a homologously recombinant cell comprising the transcription unit. The specification also indicates that the transcription unit comprises a targeting sequence, a regulatory sequence, an exon and an unpaired splice donor site, and the new transcription unit can be used to turn on or off as desired. However, none of the above provide, nor set forth a utility for the DNA nor the encoded protein. The specification fails to provide description of the activity of the polynucleotide sequence set forth in SEQ ID NO: 4 (elected for this prosecution) or the activity of the encoded protein (SEQ ID NO: 23). There is no description or demonstration on the utility of the new transcription unit that has been used for the expression of the claimed protein of SEQ ID NO: 23, encoded by polynucleotide sequence of SEQ ID NO: 4.

The specification, on page 5, indicates that the inventors have used the method of the invention to identify nineteen novel human secreted proteins. Amino acid sequence of secreted protein disclosed in SEQ ID NO: 23 encoded by the nucleic acid of SEQ ID NO: 4 (elected sequences) are under examination. But, no biological activity has been set forth for the polynucleotide (SEQ ID NO: 4) and encoded polypeptide (SEQ ID NO: 23), other than that it "has been identified as novel human secreted protein by using the method of the invention." General uses of the polynucleotides and the encoded protein set forth in the specification pages (11, 20-21), include uses in the fundamental study such as molecular weight marker, tissue marker, chromosome mapping, propagating additional copies of the polynucleotides or expressing proteins, polypeptides, fusion proteins, determining the involvement of any of these

sequences in disease states using the subgenomic polynucleotides of the invention. These do not demonstrate a specific method of use for the specifically elected sequences. They result in the requirement of further experimentation to find the specific and substantial utility. In addition the specification indicates that nucleotide probes can be constructed and used to detect altered forms of mRNA in a diseased cells, also subgenomic polynucleotides can be used to design diagnostic tests and therapeutic compositions for diseases associated with altered expression of these genes. However, the specification does not indicate explicitly the correlation of the role of any composition comprising the protein to a specific disease treatment or prevention.

The specification at page 20 indicates that the secreted proteins can be used in assays to determine biological activities, such as cytokine, cell proliferation or cellular differentiation activities, tissue growth or regeneration, activin or inhibin, chemotactic or chemokinetic, receptor/ligand activity etc. Assays of these activities are disclosed in US 5654173. Proteins of the invention can be used in protein interaction assays, to identify ligands and binding proteins, however, the art does not disclose anything regarding the significance of said receptors. Therefore, this utility is not well established and substantial.

Similarly, assertion of use of the claimed highly conserved amino acids or domains with predicted function within a protein family as a tool to identify new family members have been made (page 12), but the specification does not indicate what would be the function of those new family members. There is no disclosure of "real world" utility associated with the polypeptides encoded by the claimed DNA. Thus, the utility is not substantial.

Claim 11 is directed to method of producing a human protein by growing a culture of cells comprising a DNA construct comprising a promoter and a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence of SEQ ID NO: 23. As discussed above the specification fails to describe the utility of the claimed protein of SEQ ID NO: 23, therefore, there is no use of the method of production of that DNA which encodes a protein, which lacks utility.

Claim 12 is directed to a method of producing a human protein by growing a culture of a homologously recombinant cell having incorporated therein a new transcription initiation unit,

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wherein new transcription initiation unit comprise in 5' to 3' order: an exogenous regulatory sequence, an exogenous exon and a splice donor site, wherein the gene of the construct comprises a nucleotide sequence set forth in SEQ ID NO: 4. As discussed above the specification fails to describe the utility of the claimed nucleic acid of SEQ ID NO: 4 encoding the protein of SEQ ID NO: 23 in a homologously recombinant cell as claimed in claim 10, therefore, there is also no use of the method of production of that protein from a homologously recombinant cell, which lacks utility.

Claims 14 –24 are directed to isolated nucleic acid molecule comprising a polynucleotide consisting of a) a polynucleotide encoding amino acids 1-203 and b) 2-203 of SEQ ID NO: 23; c) the complements of a) and b); allelic variants of the polynucleotides a), b) or c), wherein the polynucleotide encodes a polypeptide that is a serine protease inhibitor; a recombinant vector; a recombinant host cell; a recombinant method of producing the protein; polynucleotides encoding the fragments of protein; an isolated nucleic acid molecule comprising SEQ ID NO: 4 or an allelic variant thereof encoding a serine protease inhibitor polypeptide. However the specification fails to describe or demonstrate any activity of the encoded protein or fragments thereof that can be correlated with a serine protease inhibitor activity as claimed in claims 14, 21 and 24.

In the instant case, the failure of applicants to specifically identify why the claimed invention is believed to be useful renders the claimed invention deficient under 35 USC 101. No specific biological activity has been identified for the polynucleotide set forth in SEQ ID NO: 4, encoding a protein set forth in SEQ ID NO: 23 other than the fact that the protein may be secreted. The person having ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO: 23 based on its structure alone for the reasons set forth above. General statements that a composition has an unspecified biological activity or that do not explain why a composition with that activity is believed to be useful fails to set forth a "specific utility." Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) (general assertion of similarities to known compounds known to be useful without sufficient corresponding explanation why claimed compounds are believed to be similarly useful is insufficient under 35 USC 101).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-12, 14-24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an adequate written description, enablement and best mode for practicing the claimed invention.

The specification is objected to because the biological material used in the claimed process is a microorganism clone, which has been deposited with American Type Culture Association (ATCC) and has the accession number SECP120997. Since the clone is essential to the practice of the claimed invention it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the organism is not so obtainable or available, the requirement of 35 U.S.C. 112 may be satisfied by a deposit of the microorganism.

That the applicants have apparently incorporated specific references into the specification does not eliminate the issue of public availability and permanence as the vectors cited in the references and the references per se do not indicate, public availability of the starting materials in as much as the biological materials mentioned in a publication may be proprietary and not publicly available.

It is apparent that the claimed clone is essential to the claimed invention and the deposit is necessary for an adequate written description, enablement, and best mode for the claimed invention, because the specification lacks a specific description or demonstration of hundred percent reproducibility of the claimed DNA and encoded protein from the deposit. Because the

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composite deposit contain one or more of the polynucleotides encoding the secreted proteins of the invention, the deposit is not 100% reproducible (see specification page 10, paragraph 1). The specification gives a generic description of isolation of a selected clone from the deposited sample, it fails to demonstrate the selection of a single clone from the mixture of cDNA clones from the composite deposit. Thus, the specification does not disclose a repeatable process to obtain the claimed clone from the deposit.

The specification on page 10, indicates that clones containing the cDNAs of the secreted proteins were deposited on December 11, 1997, with the ATCC. Applicants should provide the full address of ATCC as to read :

American Type Culture Collection (ATCC)
Patent Depository
10801 University Boulevard
Manassas, VA 20110-2209

If the deposit was made under the terms of Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure, Applicants should state this in the specification and also required to provide a photocopy of the receipt for the certificate of deposit. It is apparent that the claimed deposit material is essential to the claimed invention and the deposit is necessary for an adequate written description and enablement for the claimed invention. The Office notes that during the pendency of this application, access to the invention will be afforded to the Commissioner upon request where all restrictions upon availability to the public will be irrevocably removed upon granting of the patent and that the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer where the deposit will be replaced if it should ever become inviable.

Claims 8-12 and 14-24 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Furthermore, the claims 14 and 24 embrace allelic variants. Claim 14(d) directs to an allelic variant of a polynucleotide of (a-c) of claim 14. Claim 24 directs to an isolated nucleic acid molecule comprising SEQ ID NO: 4 or an allelic variant thereof. The specification describes that the allelic variants of the disclosed subgenomic polynucleotides can occur and encodes

proteins, which are identical, homologous, or substantially related to amino acid sequences disclosed herein (description page 12, lines 17-19).

According to Ayala et al. (Modern Genetics, Glossary), an allele is "one of two or more alternative forms of a gene, each possessing a unique nucleotide sequence; different alleles of a given gene are usually recognized, however, by the phenotypes rather than by comparison of their nucleotide sequences." The current description has disclosed no genes, where gene means genomic DNA, comprising the coding sequence of a protein. The sequences, which are disclosed, are those of cDNA. If two cDNAs differ from each other, it is impossible to tell, without the genomic DNA in hand, whether the difference arose because of an allelic variation, transcriptional modification going from genomic DNA to mRNA, post transcriptional processing of RNA, or an error in reverse transcription of mRNA into cDNA. The nature of allelic variation makes it entirely unpredictable what might be considered an allele before the isolation of such a sequence has actually taken place. The specification does not describe what might be considered an allele of the DNA of section (a-c) of claim 14 and of claim 24 or provide any examples of the same. Since the disclosed cDNA encoding a polypeptide has not been ascribed a specific function, it does not appear that allelic variants have been isolated or identified. There are no examples of allelic sequences of the claimed DNA to which one could compare undisclosed DNA to determine if they are also alleles. For these reasons the claimed allelic variants have not been adequately described, and a person having ordinary skill in art would not recognize a specific utility for the polynucleotide and would not know how to use them.

Also, if you don't know what an allelic variant looks like, what then does a hybridized polynucleotide look like. Therefore, polynucleotides that hybridize to the allelic variants that are not described cannot be envisioned by the teachings of the specification.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

"The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

Claims 8-12, 14 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite because of using the term "portion." It is unclear what that portion of a human protein is, what is the structure and function of the portion of the protein?

Claims 8-10, 12 are indefinite. The use of word "shown" renders the claim indefinite. A correction as to read "of" or "set forth" instead is suggested." It is not clear whether the compounds screened would promote the activity of the protein or they would inhibit the activity of the protein.

Claim 11 is indefinite. The use of phrase "sequence SEQ ID NO:" renders the claim indefinite. A correction as to read "sequence of SEQ ID NO:" instead is suggested."

Claims 14 and 21 are indefinite as to "about 1 to about 206" and "about 2 to about 206." It is not clear whether the amino acid sequence of the fragment includes the residue at position 1 and/or position 206 of SEQ ID NO: 23; or includes the residue at position 2 and/or position 206 of SEQ ID NO: 23. The specification fails to give a definition of the phrase "about 1 to about 206" and "about 2 to about 206."

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 8, 9 and 11 are rejected under 35 USC 102(a) as being anticipated by Bonaldo et al. (Genome Res., vol. 6, No. 9, pp. 791-806, 1996). Bonaldo et al. teach a method developed for use to generate normalized cDNA libraries from human, mouse, rat and parasites. Bonaldo's cDNA encodes a protein having 81% sequence identity to amino acid sequence of SEQ ID NO:

23 (see Bonaldo et al., "NIH_MGC_210 Homo sapiens cDNA clone, 5' mRNA sequence," August 6, 2003, alignment result 14 in frame search, EST database, Accession NO: CF146773). Bonaldo et al. also teach cDNA cloning, by reverse transcribing the poly(A) RNA prepared from various tissues (see Table 1) followed by sub-cloning of cDNA fragments using Lafmid BA vector and pT7T3-Pac vector (page 802, col. 1, first paragraph) that was transfected into E. coli DH5alpha host cells and culture was harvested (see page 802, col. 2). Bonaldo's cDNA construct is considered for an analog of the DNA construct for expressing a portion of a human protein having an amino acid sequence of SEQ ID NO: 23 thus anticipating claims 8, 9 and 11.

Claim 10 and 24 are rejected under 35 USC 102(a) as being anticipated by Shimomura et al. (J. Biol. Chem., vol. 272, No. 10, pp. 6370-6276, March 7, 1997). Shimomura et al. teach a serine protease inhibitor, designated as hepatocyte growth factor (HGF) activator inhibitor (HAI). The sequence of the cDNA revealed that the inhibitor has two well defined Kunitz domains, suggesting that the inhibitor is a member of the Kunitz family of serine protease inhibitors. The reference also teach that the inhibitory activity toward HGF activator was detected in the membrane fraction as well as in the conditioned medium of MKN45 cells, suggesting that the inhibitor may be produced as a membrane-associated form and secreted by the producing cells as a proteolytically truncated form (see abstract and page 6370, col. 2). Shimomura's cDNA has 89.3% sequence identity to nucleotide sequence of SEQ ID NO: 4 (see Shimomura et al., "Homosapiens mRNA for hepatocyte growth factor activator inhibitor, complete cds.," March 4, 1998, alignment result 14, GenEmbl database, Accession NO: AB000095). Shimomura et al. also teach cDNA cloning, by reverse transcribing the poly(A) RNA prepared from MKN45 cells followed by sub-cloning of cDNA fragments using appropriate vector, host cells (see page 6371, col. 2 and page 6372, col. 1). Shimomura's cDNA is considered for an analog and a fragment of the nucleotide sequence of SEQ ID NO: 4 thus anticipating claim 10.

Conclusion

No claim is allowed.

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Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (571) 272-0951. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547.



Rita Mitra, Ph.D.

June 23, 2004



ROBERT A. WAX
PRIMARY EXAMINER